CLAIMS:

1. A monoclonal antibody that is capable of binding specifically to wild-type HBsAg and to at least two mutant forms of HBsAg.

2. A monoclonal antibody as claimed in claim 1, wherein a mutant form of HBsAg has at least one amino acid substitution relative to wild type HBsAg.

3. A monoclonal antibody as claimed in claim 1 or claim 2, wherein a mutant form of HBsAg has the sequence of HBsAg present in an HBV escape mutant.

4. A monoclonal antibody as claimed in any one of claims 1 to 3, wherein a mutant form of HBsAg has at least one amino acid substitution in the "a" determinant or in the region of the "a" determinant.

5. A monoclonal antibody as claimed in any one of claims 2 to 4, wherein an amino acid substitution results from a point mutation.

6. A monoclonal antibody as claimed in any one of claims 1 to 5, wherein a mutant HBsAg has an amino acid substitution within the sequence encoding amino acids 133 to 145 of HBsAg.

7. A monoclonal antibody as claimed in any one of claims 1 to 6, wherein a mutant HBsAg has an amino acid substitution relative to wild type HBsAg at any one or more of positions 133, 134, 141, 142, 143, 144 and 145.

8. A monoclonal antibody as claimed in claim 7, wherein the substitution is at any one or more of positions 143, 144 and 145.

9. A monoclonal antibody as claimed in claim 7, wherein the substitution is in addition to one or more other substitutions in the "a" determinant or in another region.

10. A monoclonal antibody as claimed in claim 1, which is capable of binding specifically to wild type HBsAg and to at least one of the following mutant forms of HBsAg:
Mutant HBsAg I ("NP" HBsAg): met to ile at amino acid 133; phe to his at amino acid 134; and asp to val at amino acid 144;
Mutant HBsAg II ("MAM" HBsAg): met to ile at amino acid 133;

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phe to asn at amino acid 134; pro to ser at amino acid 142; ser to leu at amino acid 143; and gly to lys at amino acid 145;

Mutant HBsAg III ("SZ" HBsAg): gly to arg at amino acid 145;

Mutant HBsAg IV ("SP" HBsAg): ser to met at amino acid 143.

11. A monoclonal antibody that is capable of binding specifically to wild-type HBsAg and to at least one mutant HBsAg carrying an "a" determinant coded for by sequences having point mutations at any one or more of the codons encoding amino acids 143, 144 and 145.

12. A monoclonal antibody as claimed in any one of claims 1 to 11 that is an IgG, IgM or IgA immunoglobulin.

13. Monoclonal antibody P2D3 as produced by the hybridoma designated P2D3 and deposited at the ECACC under accession number ECACC 97042331.

14. Monoclonal antibody M3A10 as produced by the hybridoma designated M3A10 and deposited at the ECACC under accession number ECACC 97042330.

15. Monoclonal antibody M4F5 as produced by the hybridoma designated M4F5 and deposited at the ECACC under accession number ECACC 97042519.

16. A monoclonal antibody as claimed in any one of claims 1 to 15, in a humanised form.

17. A fragment or a derivative of a monoclonal antibody as claimed in any one of claims 1 to 16.

18. A method of producing a hybridoma capable of producing a monoclonal antibody as claimed in claim 1, which comprises immunising an animal with wild type HBsAg or a mutant form of HBsAg antigen, optionally in the form of an appropriate antigenic fragment or derivative thereof, immortalising antibody producing cells to form hybridomas, screening the hybridoma cultures against wild type HBsAg and two or more mutant forms of HBsAg, optionally in the form of an appropriate antigenic fragment or derivative thereof, and selecting those hybridomas that produce antibodies that bind to wild type HBsAg and two or more mutant forms of HBsAg.

19. A method as claimed in claim 18, wherein a mutant form

of HBsAg is as defined in any one of claims 2 to 11.

20. A hybridoma capable of producing a monoclonal antibody as claimed in any one of claims 1 to 11.

21. Hybridoma designated P2D3 and deposited at the ECACC under accession number ECACC 97042331.

22. Hybridoma designated M3A10 and deposited at the ECACC under accession number ECACC 97042330.

23. Hybridoma designated M4F5 and deposited at the ECACC under accession number ECACC 97042519.

24. A method of producing a monoclonal antibody as claimed in claim 1, which comprises culturing a hybridoma as claimed in any one of claims 20 to 23 or obtainable by a method as claimed in claim 18 or claim 19 in vitro or in vivo, and obtaining the monoclonal antibody from the culture medium.

25. A monoclonal antibody obtainable by the method claimed in claim 24.

26. An immunoassay for the detection of HBsAg, which comprises contacting a sample under investigation with a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a fragment or derivative thereof as claimed in claim 17, or a combination of two or more thereof, and detecting any resulting antigen-antibody complex.

27. An immunoassay as claimed in claim 26, wherein the monoclonal antibody, fragment, derivative or combination thereof is used in combination with one or more other antibodies selected from polyclonal anti-HBs antibodies and other monoclonal anti-HBs antibodies.

28. An immunoassay as claimed in claim 26 or claim 27, in a homogeneous or heterogeneous format.

29. An immunoassay as claimed in claim 28, in a capture or a competitive format.

30. An immunoassay as claimed in any one of claims 26 to 29, wherein an immunoassay for the detection of antibodies to hepatitis B core protein (HBc) is carried out simultaneously with the assay for HBsAg.

31. An immunoassay kit that comprises a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a

fragment or derivative thereof as claimed in claim 17, or a combination of two or more thereof, and other reagents required for carrying out an immunoassay for HBsAg and optionally also reagents for detecting anti-HBc antibodies.

32. A kit as claimed in claim 31, which also comprises one or more other anti-HBs antibodies selected from polyclonal anti-HBs antibodies and other monoclonal anti-HBs antibodies.

33. A kit as claimed in claim 31 or claim 32, wherein the other reagents are selected from washing solutions, diluents, standard solutions, control reagents and labelled anti-HBs antibodies.

34. A solid phase suitable for use in an immunoassay on which is immobilised a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a fragment or derivative thereof as claimed in claim 17, or a combination of two or more thereof.

35. A solid phase as claimed in claim 34, wherein one or more further anti-HBs antibodies selected from polyclonal anti-HBs antibodies and other monoclonal anti-HBs antibodies are also immobilised on the solid phase.

36. A solid phase as claimed in claim 34 or claim 35, on which is also immobilised an agent capable of capturing anti-HBc antibodies.

37. An antiserum suitable for use therapeutically or prophylactically for passive immunisation which comprises a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a fragment or derivative as claimed in claim 17, or a combination of two or more thereof.

38. A composition suitable for use therapeutically or prophylactically for passive immunisation against HBV which comprises a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a fragment or derivative as claimed in claim 17, or a combination of two or more thereof, in admixture with a pharmaceutically suitable carrier.

39. An antiserum as claimed in claim 37 or a composition as claimed in claim 38, which also comprises one or more other antibodies selected from polyclonal anti-HBs antibodies and

other monoclonal anti-HBs antibodies.

40. A method of therapeutic or prophylactic passive immunisation against HBV infection, which comprises administering to a subject a therapeutically or prophylactically effective amount of a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, a fragment or derivative as claimed in claim 17, or a combination of two or more thereof.

41. A method as claimed in claim 40, wherein one or more other antibodies selected from monoclonal and polyclonal anti-HBs antibodies are also administered.

42. An anti-idiotype antibody to a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25, or a fragment or derivative thereof as claimed in claim 17.

43. Isolated Mutant HBsAG I, Mutant HBsAG II, Mutant HBsAG III or Mutant HBsAG IV as defined in claim 10.

44. A mutant HBsAg as claimed in claim 43, obtainable from a natural source.

45. A mutant HBsAg as claimed in 43, obtainable recombinantly.

46. A mutant HBsAg as claimed in claim 45, being glycosylated.

47. A fragment or derivative of a mutant HBsAg as claimed in any one of claims 43 to 46, said fragment or derivative being capable of binding specifically to a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25 or to a fragment or derivative as claimed in claim 17.

48. A fragment or derivative as claimed in claim 47, said fragment or derivative being immunogenic.

49. A vaccine composition that comprises a mutant HBsAg as claimed in any one of claims 43 to 46 or a fragment or derivative as claimed in claim 48, or a combination of two or more thereof, and a pharmaceutically suitable carrier.

50. A vaccine composition as claimed in claim 49, which further comprises one or more other immunogenic peptides or polypeptides.

51. A vaccine composition as claimed in claim 50, wherein

the immunogenic peptides or polypeptides are immunogenic HBsAG peptides or polypeptides.

52. A method of vaccinating a subject against HBV, which comprises administering to the subject a therapeutically effective amount of a mutant HBsAg as claimed in any one of claims 43 to 46, a fragment or derivative as claimed in claim 48, or a combination of two or more thereof, optionally in combination with one or more other immunogenic HBsAg peptides or polypeptides.

53. An isolated nucleic acid that encodes Mutant HBsAG I, Mutant HBsAG II, Mutant HBsAG III or Mutant HBsAG IV as defined in claim 10.

54. A nucleic acid that encodes a fragment or derivative of a mutant HBsAg as defined in claim 10, said fragment or derivative being capable of binding specifically to a monoclonal antibody as claimed in any one of claims 1 to 16 or claim 25 or to a fragment or derivative thereof as claimed in claim 17.

55. A nucleic acid as claimed in claim 54, wherein the fragment or derivative of the mutant HBsAg is immunogenic.

56. A composition that comprises a nucleic acid as claimed in any one of claims 53 to 55.

57. A vaccine composition that comprises a nucleic acid as claimed in claim 53 or claim 55 in a form suitable for expression of the encoded amino acid sequence when administered to a mammal.

58. A method of vaccination against HBV, which comprises administering to a subject a therapeutically or prophylactically effective amount of a nucleic acid as claimed in claim 53 or claim 57 or a vaccine composition as claimed in claim 57.

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